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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,289	12/12/2003	Jing Zhu	1676.011US1	9939

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EXAMINER	
HAMUD, FOZIA M	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,289	ZHU ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *47-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/11/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restriction:

1a. Applicant's election with traverse of Group I, claims 1-46, (drawn in part to a method of administering to a mammal a proepithelin (PEPI), alone or with secretory leukocyte protease inhibitor (SLPI), wherein said PEPI comprises the amino acid sequence set forth in SEQ ID NO:1 and the SLPI comprises the amino acid sequence set forth in SEQ ID NO:7, is acknowledged.

The traversal is on the grounds that searching and examining of at least several of the groups would not be burdensome. Applicants also submit that restriction into twenty different groups based on minor sequence differences makes each species of PEPI or SLPI a separate invention. Applicants imply that species election would have been more appropriate. Finally, Applicants contend that the only difference between Group I and Group II is that SEQ ID NO:1 of Group I differs from SEQ ID NO:2 of Group II by only one amino acid residue.

This traversal has been considered, but is deemed persuasive only in part. It appears that the polypeptides of SEQ ID Nos: 1 and 2 are related and the polypeptide of SEQ ID Nos: 4 and 5 are also related. Accordingly, Groups that include SEQ ID Nos: 1 and 2 will be combined together, and Groups that include SEQ ID Nos: 4 and 5 will also be combined. Thus, new groups of the claimed invention, follows:

I. Claims 1-46, drawn in part, to a method of administering to a mammal a proepithelin (PEPI), alone or with secretory leukocyte protease inhibitor (SLPI), wherein said PEPI comprises the amino acid sequence set forth in SEQ ID NO:1,

or 2 and the SLPI comprises the amino acid sequence set forth in SEQ ID NO:7, classified in class, 514, subclass 12.

II. Claims 1-46, drawn in part, to a method of administering to a mammal a proepithelin (PEPI), alone or with a secretory leukocyte protease inhibitor (SLPI), wherein said PEPI comprises the amino acid sequence set forth in SEQ ID NO:1 or 2, and the SLPI comprises the amino acid sequence set forth in SEQ ID NO:9, classified in class, 514, subclass 12.

III Claims 1-46, drawn in part, to a method of administering to a mammal a proepithelin (PEPI), alone or with secretory leukocyte protease inhibitor (SLPI), wherein said PEPI comprises the amino acid sequence set forth in SEQ ID NO:4 or 5, and the SLPI comprises the amino acid sequence set forth in SEQ ID NO:7, classified in class, 514, subclass 12.

IV. Claims 1-46, drawn in part, to a method of administering to a mammal a proepithelin (PEPI), alone or with a secretory leukocyte protease inhibitor (SLPI), wherein said PEPI comprises the amino acid sequence set forth in SEQ ID NO:4 or 5 and the SLPI comprises the amino acid sequence set forth in SEQ ID NO:9, classified in class, 514, subclass 12.

V. Claims 47-51, drawn in part, to a to a composition comprising a proepithelin (PEPI), which comprises the amino acid set forth in SEQ ID NO:1 or 2, classified in class, 530, subclass 351.

VI. Claims 47-51, drawn in part, to a to a composition comprising a proepithelin (PEPI), which comprises the amino acid set forth in SEQ ID NO:4 or 5, classified in class, 530, subclass 351.

VII. Claims 52-57, drawn in part, to a composition comprising a proepithelin (PEPI), which comprises the amino acid sequence set forth in SEQ ID NO:1 or 2, and an SLPI which comprises the amino acid sequence set forth in SEQ ID NO:7, classified in class, 530, subclass 351.

VIII. Claims 52-57, drawn in part, to a composition comprising a proepithelin (PEPI), which comprises the amino acid sequence set forth in SEQ ID NO:1 or 2, and an SLPI which comprises the amino acid sequence set forth in SEQ ID NO:9, classified in class, 530, subclass 351.

IX. Claims 52-57, drawn in part, to a composition comprising a proepithelin (PEPI), which comprises the amino acid sequence set forth in SEQ ID NO:4 or 5 and an SLPI which comprises the amino acid sequence set forth in SEQ ID NO:7, classified in class, 530, subclass 351.

X. Claims 52-57, drawn in part, to a composition comprising a proepithelin (PEPI), which comprises the amino acid sequence set forth in SEQ ID NO:4 or 5, and an SLPI which comprises the amino acid sequence set forth in SEQ ID NO:9, classified in class, 530, subclass 351.

The polypeptides of SEQ ID Nos: 1, 2, are human while those of SEQ ID Nos: 4, 5 are mouse. It appears that the human sequence share a great deal of homology, however, that these human sequence are distinct from the mouse sequences. Likewise,

SEQ ID NO:7 and SEQ ID NO:9 appear not to be related. A search for the human sequences would not reveal art pertinent to the mouse sequences. Therefore, searching all of the sequences would be burdensome. This is not a species election, but rather a restriction requirement.

Status of Claims:

1b. Claims 1-57 are pending, of which claims 1-46, are drawn to the elected invention in part. Claims 1-46, will be searched and examined insofar as they pertain to a method of administering to a mammal a proepithelin (PEPI), alone or with secretory leukocyte protease inhibitor (SLPI), wherein said PEPI comprises the amino acid sequence set forth in SEQ ID NO:1, or 2 and the SLPI comprises the amino acid sequence set forth in SEQ ID NO:7. Claims 47-57 are withdrawn from consideration by the Examiner as they are drawn to non-elected invention.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted 12 April 2004 has been received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Specification:

3a. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3b. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, on page 9, line 25. Applicant is required to

delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections:

4a. Claims 3, 4, 6, 26, 27, 29 are objected to because of the following informalities: these claims recite non-elected sequences. Appropriate correction is required.

Claim rejections-35 USC § 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of wound healing in a mammal by administering the proepithelin polypeptide (PEPI) comprising the amino acid sequence set forth in SEQ ID NO:1 or 2 in combination with the secretory leukocyte protease inhibitor (SLPI) comprising the amino acid sequence set forth in SEQ ID NO:7, does not reasonably provide enablement for a method of enhancing wound healing in a mammal by administering PEPI subunit or "all possible" proepithelin polypeptide (PEPI) and SLPI subunit or "all possible" secretory leukocyte protease inhibitor (SLPI). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, practice the invention commensurate in scope with these claims.

Claims 1-2 and 24-25 encompass a method of enhancing wound healing or a method of inhibiting inflammation in a mammal afflicted with a wound by administering

PEPI or subunit thereof, alone or in combination with SLPI or subunit thereof. However, the instant specification discloses that SLPI and proeptihelin form complexes, which prevents elastase from converting proepithelin to epithelins, (see page 2, lines 25-31). The specification further discloses that while, epithelins inhibit the growth of epithelial cells and induce the proinflammaotry cytokine IL-8, proepiothelin blocks TNF induced neutrophil activation and prevents the release of oxidants and proteases, (see pages 2-3). Thus, the specification only discloses that the interaction between PEPI and SLPI inhibits the conversion or digestion of proepithelin to epithelin, and thus does not enable using PEPI alone to enhance wound healing. Furthermore, the claims broadly encompass "all possible PEPI" as well as "all possible SLPI", however, the specification only discloses the PEPI comprising the amino acid sequence set forth in SEQ ID NO:1, 2 and SLPI comprising the amino acid sequence set forth in SEQ ID NO:7, and is therefore, non-enabling for the unlimited number of PEPI or SLPI proteins which are encompassed by the scope of the claims. The claimed invention encompasses administering PEPI or SLPI proteins not envisioned or described in the specification, and neither does the specification disclose how these PEPI or SLPI proteins can be distinguished from each other. The specification only enables administering the PEPI of SEQ ID NO:1 or 2 together with the SLPI of SEQ ID NO:7, the polypeptides having specific characteristics and properties. These properties may differ structurally, chemically and physically from other known PEPI or SLPI proteins. Regarding the recitation of "subunit thereof", the specification does not disclose that a subunit of PEPI alone or in combination with SLPI or subunit of SLPI enhances wound healing or inhibits

inflammation. The specification teaches that epithelins (EPIs), which are derived from proepithelin, inhibit the growth of epithelial cells and induce the proinflammaotry cytokine IL-8, while proepiothelin blocks TNF induced neutrophil activation and prevents the release of oxidants and proteases. Thus, EPIs, which are subunits of proepithelin have an opposing effect as proepithelin, and therefore, would not be expected to enhance wound healing.

The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination, in the instant application, the quantity of experimentation to determine all the PEPI or subunits and SLPI or subunits encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little. Therefore, it would require undue experimentation to determine whether all the PEPI or subunits and SLPI or subunits would be encompassed by the scope of the claims would retain the desired activity. The disclosure that administering the PEPI comprising the amino acid sequence set forth in SEQ ID NO:1, 2 in combination with the SLPI comprising the amino acid sequence set forth in SEQ ID NO:7, is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass the administration of "all possible" PEPI or

subunits and "all possible" SLPI or subunits, including mutants thereof. Furthermore, the amount of embodiments corresponding to the desirable compositions, may be innumerable, and the enabled embodiment amount to only the administration of PEPI of SEQ ID NO:1, 2, together with the SLPI of SEQ ID NO:7. Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Therefore, Applicants are not enabled for a method of administering PEPI or subunits thereof, alone, or a method of administering "all possible" PEPIs in combination with "all possible" SLPI or subunits to enhance wound healing or inhibit inflammation. The specification only enables a method of wound healing in a mammal by administering the proepithelin polypeptide (PEPI) comprising the amino acid sequence set forth in SEQ ID NO:1 or 2 in combination with the secretory leukocyte protease inhibitor (SLPI) comprising the amino acid sequence set forth in SEQ ID NO:7.

Conclusion:

5. No claim is allowed.

The claims are free of prior art of record. At the time the instant application was filed, it was known that secretory leukocyte protease inhibitor (SLPI) has an important role in cutaneous wound healing, in part because it inhibits local elastases, (see Ashcroft et al, nature Medicine, October 2000, Vol. 6, No.10, pages 1147-1153, especially page 1151, column 2; cited on the IDS submitted on 11 March 2004). It was also known that epithelin/granulin precursor is derived from PC cells (moderately

tumorgenic cell line) and may act as a high molecular weight growth factor for these cells, (see Bateman et al, Journal of Endocrinology, 1998, Vol. 158, pages 145-151, especially page 148, column 2, also cited on the IDS submitted on 11 March 2004). However, the prior art neither discloses nor suggests that proeptihelin forms a complex with SLPI, which prevents elastase from converting proepithelin to epithelins, thereby, preventing the release of oxidants and proteases, which inhibits inflammation and enhances wound healing.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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26 March 2007

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